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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28	Oct 21	EVENTLINE has been reloaded
NEWS 29	Oct 24	BEILSTEIN adds new search fields
NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 32	Nov 18	DKILIT has been renamed APOLLIT
NEWS 33	Nov 25	More calculated properties added to REGISTRY
NEWS 34	Dec 02	TIBKAT will be removed from STN
NEWS 35	Dec 04	CSA files on STN
NEWS 36	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 37	Dec 17	TOXCENTER enhanced with additional content
NEWS 38	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 39	Dec 30	ISMEC no longer available

NEWS EXPRESS	December 31 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 12:47:48 ON 06 JAN 2003

=> file biosis medline agricola embase caba wpids japio biotechds lifesci caplus uspatall
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FULL ESTIMATED COST 0.21 0.21

FILE 'BIOSIS' ENTERED AT 12:48:32 ON 06 JAN 2003
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FILE 'USPATFULL' ENTERED AT 12:48:32 ON 06 JAN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 12:48:32 ON 06 JAN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> e leonard jon p/au
E1 4 LEONARD JON/AU
E2 5 LEONARD JON N/AU
E3 0 --> LEONARD JON P/AU
E4 6 LEONARD JONATHAN/AU
E5 5 LEONARD JONATHAN B/AU

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E7            3      LEONARD JONATHAN H/AU
E8            6      LEONARD JONATHAN N/AU
E9            3      LEONARD JONATHAN NORTON/AU
E10           1      LEONARD JONATHAN NORTON 1903/AU
E11          12      LEONARD JONATHAN S/AU
E12           2      LEONARD JONES J E/AU

=> e leonard john p/au
E1           79      LEONARD JOHN M/AU
E2            3      LEONARD JOHN N/AU
E3          118 --> LEONARD JOHN P/AU
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E5            1      LEONARD JOHN PAUL/AU
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E8            1      LEONARD JOHN T/AU
E9            1      LEONARD JOHN W JR/AU
E10           1      LEONARD JOHNATAN N/AU
E11           1      LEONARD JOHNSON F/AU
E12           4      LEONARD JON/AU

=> s e3-e5
L1          120 ("LEONARD JOHN P"/AU OR "LEONARD JOHN PATRICK"/AU OR "LEONARD
                JOHN PAUL"/AU)

=> e goldman samuel/au
E1            2      GOLDMAN S Z/AU
E2            1      GOLDMAN SAM/AU
E3           14 --> GOLDMAN SAMUEL/AU
E4            6      GOLDMAN SAMUEL C/AU
E5            1      GOLDMAN SAMUEL D/AU
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E9            7      GOLDMAN SAMUEL M/AU
E10           1      GOLDMAN SANDY/AU
E11           6      GOLDMAN SARAH/AU
E12           2      GOLDMAN SARAH A/AU

=> s e3
L2           14 "GOLDMAN SAMUEL"/AU

=> e goldman s/au
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E2            1      GOLDMAN RUVIN/AU
E3         1469 --> GOLDMAN S/AU
E4          258      GOLDMAN S A/AU
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E10          15      GOLDMAN S F/AU
E11           9      GOLDMAN S G/AU
E12          11      GOLDMAN S H/AU

=> s e3
L3         1469 "GOLDMAN S"/AU

=> e ohara richard/au
E1            1      OHARA REIJI/AU
E2           21      OHARA REIKO/AU
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E3           0 --> OHARA RICHARD/AU
E4           1     OHARA RIE/AU
E5           1     OHARA RIEKO/AU
E6         107     OHARA RIICHIRO/AU
E7           1     OHARA RIKURO/AU
E8           1     OHARA RURI/AU
E9           4     OHARA RYO/AU
E10         14     OHARA RYOICHI/AU
E11          1     OHARA RYOUICHI/AU
E12          2     OHARA RYUICHI/AU

=> e o'hara richard/au
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
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MISMATCHED QUOTE IN EXPAND TERM
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
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=> e ohara richard/au
E1           1     OHARA REIJI/AU
E2          21     OHARA REIKO/AU
E3           0 --> OHARA RICHARD/AU
E4           1     OHARA RIE/AU
E5           1     OHARA RIEKO/AU
E6         107     OHARA RIICHIRO/AU
E7           1     OHARA RIKURO/AU
E8           1     OHARA RURI/AU
E9           4     OHARA RYO/AU
E10         14     OHARA RYOICHI/AU
E11          1     OHARA RYOUICHI/AU
E12          2     OHARA RYUICHI/AU

=> e ohara r/au
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E2          20     OHARA PETER T/AU
E3          71 --> OHARA R/AU
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E6           4     OHARA R J/AU
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E9           1     OHARA REIJI/AU
E10         21     OHARA REIKO/AU
E11          1     OHARA RIE/AU
E12          1     OHARA RIEKO/AU

=> s e3
L4          71 "OHARA R"/AU

=> d his

     (FILE 'HOME' ENTERED AT 12:47:48 ON 06 JAN 2003)
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FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 12:48:32 ON 06 JAN 2003

E LEONARD JON P/AU
E LEONARD JOHN P/AU
L1 120 S E3-E5
E GOLDMAN SAMUEL/AU
L2 14 S E3
E GOLDMAN S/AU
L3 1469 S E3
E OHARA RICHARD/AU
E OHARA RICHARD/AU
E OHARA R/AU
L4 71 S E3

=> s l1-l4
L5 1672 (L1 OR L2 OR L3 OR L4)

=> s l5 and rhemuatoid arthritis
L6 0 L5 AND RHEMUATOID ARTHRITIS

=> s l5 and rheumatoid arthritis
L7 15 L5 AND RHEUMATOID ARTHRITIS

=> s l7 and il-12
L8 5 L7 AND IL-12

=> sl7 and il-12 (5a) antagonist
SL7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l7 and il-12 (5a) antagonist
L9 3 L7 AND IL-12 (5A) ANTAGONIST

=> d bib ab 1-3

L9 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:166945 BIOSIS
DN PREV200200166945
TI Use of IL-12 and IL-12 antagonists in the treatment of autoimmune diseases.
AU Leonard, John (1); **Goldman, Samuel**; O'Hara, Richard, Jr.
CS (1) Auburn, NH USA
ASSIGNEE: Genetics Institute, Inc.
PI US 6338848 January 15, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 15, 2002) Vol. 1254, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB Method of treating autoimmune conditions are disclosed comprising administering to a mammalian subject **IL-12** or an **IL-12 antagonist**. In certain preferred embodiments the autoimmune condition is one which is promoted by an increase in levels of IFN-gamma or TNF-alpha. Suitable conditions for treatment include multiple sclerosis, systemic lupus erythematosus, **rheumatoid arthritis**, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes melitis and autoimmune inflammatory eye disease.

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

AN 1995:934127 CAPLUS
DN 123:337469
TI Use of IL-12 and IL-12 antagonists in treatment of autoimmune diseases
IN **Leonard, John P.**; **Goldman, Samuel**; O'Hara, Richard, Jr.
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524918	A1	19950921	WO 1995-US2550	19950307
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9500960	A	19951010	ZA 1995-960	19950207
	TW 400233	B	20000801	TW 1995-84101380	19950214
	IL 112677	A1	20000131	IL 1995-112677	19950216
	CA 2185565	AA	19950921	CA 1995-2185565	19950307
	AU 9519749	A1	19951003	AU 1995-19749	19950307
	AU 689236	B2	19980326		
	EP 750509	A1	19970102	EP 1995-912666	19950307
	EP 750509	B1	20020515		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510444	T2	19971021	JP 1995-524044	19950307
	EP 1179348	A2	20020213	EP 2001-117762	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 217533	E	20020615	AT 1995-912666	19950307
	ES 2173953	T3	20021101	ES 1995-912666	19950307
	US 6338848	B1	20020115	US 2000-513380	20000225
PRAI	US 1994-212629	A	19940314		
	EP 1995-912666	A3	19950307		
	WO 1995-US2550	W	19950307		
	US 1995-560943	B1	19951120		

AB Autoimmune conditions such as multiple sclerosis, systemic lupus erythematosus, **rheumatoid arthritis**, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin-dependent diabetes mellitus, and autoimmune inflammatory eye disease, esp. conditions which are promoted by an increase in levels of IFN-.gamma. or TNF-.alpha., are treated in mammals by administering **IL-12** or an **IL-12 antagonist**. Thus, lymphocytes from mice immunized with myelin proteolipid protein, and restimulated with a synthetic peptide from this protein, were injected into naive mice. The injected mice developed exptl. allergic encephalomyelitis which was exacerbated by incubation of these lymphocytes with IL-12 during restimulation, and alleviated by injection of a polyclonal antibody to IL-12.

L9 ANSWER 3 OF 3 USPATFULL
AN 2002:9647 USPATFULL
TI Use of IL-12 and IL-12 antagonists in the treatment of autoimmune diseases
IN Leonard, John, Auburn, NH, United States
Goldman, Samuel, Acton, MA, United States
O'Hara, Jr., Richard, Quincy, MA, United States
PA Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6338848 B1 20020115
AI US 2000-513380 20000225 (9)
RLI Continuation of Ser. No. US 1995-560943, filed on 20 Nov 1995, now abandoned Continuation of Ser. No. US 1994-212629, filed on 14 Mar 1994, now abandoned

DT Utility
FS GRANTED
EXNAM Primary Examiner: Minnifield, Nita M.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 676
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method of treating autoimmune conditions are disclosed comprising administering to a mammalian subject **IL-12** or an **IL-12 antagonist**. In certain preferred embodiments the autoimmune condition is one which is promoted by an increase in levels of IFN-.gamma. or TNF-.alpha.. Suitable conditions for treatment include multiple sclerosis, systemic lupus erythematosus, **rheumatoid arthritis**, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes melitis and autoimmune inflammatory eye disease.

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		E	LEONARD JOHN P/AU
L1	120	S	E3-E5
		E	GOLDMAN SAMUEL/AU
L2	14	S	E3
		E	GOLDMAN S/AU
L3	1469	S	E3
		E	OHARA RICHARD/AU
		E	OHARA RICHARD/AU
		E	OHARA R/AU
L4	71	S	E3
L5	1672	S	L1-L4
L6	0	S	L5 AND RHEMUATOID ARTHRITIS
L7	15	S	L5 AND RHEUMATOID ARTHRITIS
L8	5	S	L7 AND IL-12
L9	3	S	L7 AND IL-12 (5A) ANTAGONIST

=> dup rem l8
PROCESSING COMPLETED FOR L8
L10 4 DUP REM L8 (1 DUPLICATE REMOVED)

=> d bib 1-4

L10 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:166945 BIOSIS
DN PREV200200166945
TI Use of **IL-12** and **IL-12** antagonists in the treatment of autoimmune diseases.
AU Leonard, John (1); **Goldman, Samuel**; O'Hara, Richard, Jr.
CS (1) Auburn, NH USA
ASSIGNEE: Genetics Institute, Inc.
PI US 6338848 January 15, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 15, 2002) Vol. 1254, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133.
DT Patent

LA English

L10 ANSWER 2 OF 4 USPATFULL
AN 2000:74115 USPATFULL
TI Polynucleotides encoding human CTLA-8 related proteins
IN Jacobs, Kenneth, Newton, MA, United States
Kelleher, Kerry, Marlborough, MA, United States
Carlin, McKeough, Cambridge, MA, United States
Goldman, Samuel, Acton, MA, United States
Pittman, Debra, Windham, NH, United States
Mi, Sha, Belmont, MA, United States
Neben, Steven, Acton, MA, United States
Giannotti, Joanne, Acton, MA, United States
Golden-Fleet, Margaret M., Medford, MA, United States
PA Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6074849 20000613
AI US 1996-685239 19960718 (8)
RLI Continuation-in-part of Ser. No. US 1995-514014, filed on 11 Aug 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1658
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 3 OF 4 USPATFULL
AN 2000:37900 USPATFULL
TI Human CTLA-8 and uses of CTLA-8-related proteins
IN Jacobs, Kenneth, Newton, MA, United States
Kelleher, Kerry, Marlborough, MA, United States
Carlin, McKeough, Cambridge, MA, United States
Goldman, Samuel, Acton, MA, United States
Pittman, Debra, Windham, NH, United States
Mi, Sha, Belmont, MA, United States
Neben, Steven, Acton, MA, United States
Giannotti, Joanne, Acton, MA, United States
Golden-Fleet, Margaret M., Medford, MA, United States
PA Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6043344 20000328
AI US 1998-34810 19980304 (9)
RLI Division of Ser. No. US 1996-685239, filed on 18 Jul 1996, now abandoned which is a continuation-in-part of Ser. No. US 1995-504032, filed on 19 Jul 1995 which is a continuation-in-part of Ser. No. US 1995-514014, filed on 11 Aug 1995, now patented, Pat. No. US 5707829
PRAI US 1995-35347P 19950719 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Lahive & Cockfield, LLP, Mandragouras, Esq., Amy E., Lauro, Esq., Peter C.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1761
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1995:934127 CAPLUS

DN 123:337469
TI Use of **IL-12** and **IL-12** antagonists in treatment of autoimmune diseases
IN **Leonard, John P.**; **Goldman, Samuel**; O'Hara, Richard, Jr.
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524918	A1	19950921	WO 1995-US2550	19950307
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9500960	A	19951010	ZA 1995-960	19950207
	TW 400233	B	20000801	TW 1995-84101380	19950214
	IL 112677	A1	20000131	IL 1995-112677	19950216
	CA 2185565	AA	19950921	CA 1995-2185565	19950307
	AU 9519749	A1	19951003	AU 1995-19749	19950307
	AU 689236	B2	19980326		
	EP 750509	A1	19970102	EP 1995-912666	19950307
	EP 750509	B1	20020515		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510444	T2	19971021	JP 1995-524044	19950307
	EP 1179348	A2	20020213	EP 2001-117762	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 217533	E	20020615	AT 1995-912666	19950307
	ES 2173953	T3	20021101	ES 1995-912666	19950307
	US 6338848	B1	20020115	US 2000-513380	20000225
PRAI	US 1994-212629	A	19940314		
	EP 1995-912666	A3	19950307		
	WO 1995-US2550	W	19950307		
	US 1995-560943	B1	19951120		

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=> s rheumatoid arthritis
L11     189113 RHEUMATOID ARTHRITIS

=> s il-12 antagonist?
L12        126 IL-12 ANTAGONIST?

=> s l12 and antibod?
L13         49 L12 AND ANTIBOD?

=> s l11 and l13
L14         18 L11 AND L13

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15          16 DUP REM L14 (2 DUPLICATES REMOVED)

=> d bib ab 1-16

L15  ANSWER 1 OF 16  USPATFULL
AN     2002:133211  USPATFULL
TI     Cytokine antagonists
IN     Debets, Johannes Eduard Maria Antonius, Rhoon, NETHERLANDS
       Abrams, John S., Los Altos, CA, UNITED STATES
       Kastelein, Robert A., Redwood City, CA, UNITED STATES
       O'Garra, Anne, Palo Alto, CA, UNITED STATES
PI     US 2002068060      A1   20020606
```

AI US 2001-834295 A1 20010412 (9)
PRAI US 2000-196754P 20000412 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 862
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antagonists of a cytokine signaling system have been found which exhibit favorable properties. In particular, **antibody** antagonists raised against the receptor are effective in blocking various signaling processes.

L15 ANSWER 2 OF 16 USPATFULL
AN 2002:48631 USPATFULL
TI THERAPEUTIC COMPOUNDS FOR INHIBITING INTERLEUKIN-12 SIGNALING AND METHODS FOR USING SAME
IN KLEIN, J. PETER, VASHON, WA, UNITED STATES
KLAUS, STEPHEN J., SEATTLE, WA, UNITED STATES
KUMAR, ANIL M., MERCER ISLAND, WA, UNITED STATES
GONG, BAOQING, SHORELINE, WA, UNITED STATES
PI US 2002028823 A1 20020307
AI US 1999-288556 A1 19990409 (9)
RLI Continuation-in-part of Ser. No. US 1998-8020, filed on 16 Jan 1998, ABANDONED
DT Utility
FS APPLICATION
LREP MCDERMOTT WILL & EMERY, 600 13TH STREET, N.W., WASHINGTON, DC, 20005-3096
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 4381
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel heterocyclic compounds having a six membered ring structure fused to a five membered ring structure are found to be useful for the treatment and prevention of symptoms or manifestations associated with disorders affected by Interleukin-12 ("IL-12") intracellular signaling, such as, for example, Th1 cell-mediated disorders. The therapeutic compounds, pharmaceutically acceptable derivatives (e.g., resolved enantiomers, diastereomers, tautomers, salts and solvates thereof) or prodrugs thereof, have the following general formula: ##STR1##

Each X, Y and Z are independently selected from a member of the group consisting of C(R.sub.3), N, N(R.sub.3) and S. Each R.sub.1, R.sub.2 and R.sub.3 is substituted or unsubstituted and is independently selected from a member of the group consisting of hydrogen, halo, oxo, C.sub.(1-20)alkyl, C.sub.(1-20)hydroxyalkyl, C.sub.(1-20)thioalkyl, C.sub.(1-20)alkylamino, C.sub.(1-20)alkylaminoalkyl, C.sub.(1-20)aminoalkyl, C.sub.(1-20)aminoalkoxyalkenyl, C.sub.(1-20)aminoalkoxyalkynyl, C.sub.(1-20)diaminoalkyl, C.sub.(1-20)triaminoalkyl, C.sub.(1-20)tetraaminoalkyl, C.sub.(5-15)aminotrialkoxyamino, C.sub.(1-20)alkylamido, C.sub.(1-20)alkylamidoalkyl, C.sub.(1-20)amidoalkyl, C.sub.(1-20)acetamidoalkyl, C.sub.(1-20)alkenyl, C.sub.(1-20)alkynyl, C.sub.(3-8)alkoxyl, C.sub.(1-11)alkoxyalkyl, and C.sub.(1-20)dialkoxyalkyl.

L15 ANSWER 3 OF 16 USPATFULL
AN 2002:276097 USPATFULL

TI Method of inhibiting interleukin-12 signaling
IN Klaus, Stephen J., Seattle, WA, United States
Klein, J. Peter, Vashon Island, WA, United States
Kumar, Anil M., Mercer Island, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6469017 B1 20021022
AI US 1998-8020 19980116 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Criares, Theodore J.
LREP Foley & Lardner
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 898
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for blocking IL-12 signaling by administration of the following compound: ##STR1##

wherein, R.sub.1 is H, CH.sub.3, sulfate, phosphate, or salt thereof; R.sub.2 is alkyl (C.sub.1-12), alkoxyalkyl (C.sub.1-11), dialkoxyalkyl, CH.sub.2C.sub.6H.sub.5, --CH.sub.2-furan, biotin; and R.sub.3 is H, CH.sub.3 or CH.sub.2C.sub.6H.sub.5.

L15 ANSWER 4 OF 16 USPATFULL
AN 2002:9647 USPATFULL
TI Use of IL-12 and **IL-12 antagonists** in the treatment of autoimmune diseases
IN Leonard, John, Auburn, NH, United States
Goldman, Samuel, Acton, MA, United States
O'Hara, Jr., Richard, Quincy, MA, United States
PA Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6338848 B1 20020115
AI US 2000-513380 20000225 (9)
RLI Continuation of Ser. No. US 1995-560943, filed on 20 Nov 1995, now abandoned Continuation of Ser. No. US 1994-212629, filed on 14 Mar 1994, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Minnifield, Nita M.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 676
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method of treating autoimmune conditions are disclosed comprising administering to a mammalian subject IL-12 or an **IL-12 antagonist**. In certain preferred embodiments the autoimmune condition is one which is promoted by an increase in levels of IFN-.gamma. or TNF-.alpha.. Suitable conditions for treatment include multiple sclerosis, systemic lupus erythematosus, **rheumatoid arthritis**, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes melitis and autoimmune inflammatory eye disease.

L15 ANSWER 5 OF 16 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1
AN 2001-244697 [25] WPIDS
DNC C2001-073427
TI Modulating responsiveness to a corticosteroid by administering a corticosteroid with an agent which antagonizes a target that regulates interferon-gamma production or an caspase family protease inhibitor,

useful for treating asthma.

DC B04 B05 D16

IN BANERJEE, S; CARTER, A; GHAYUR, T; SEKUT, L; TRACEY, D E

PA (BADI) BASF AG

CYC 94

PI WO 2001019373 A2 20010322 (200125)* EN 152p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000071276 A 20010417 (200140)

ADT WO 2001019373 A2 WO 2000-US24725 20000908; AU 2000071276 A AU 2000-71276 20000908

FDT AU 2000071276 A Based on WO 200119373

PRAI US 1999-398555 19990917

AB WO 200119373 A UPAB: 20010508

NOVELTY - A new method (M1) for modulating responsiveness to a corticosteroid in a subject comprises administering a corticosteroid with an agent (A1) which antagonizes a target that regulates production of interferon-gamma (IFN-gamma) or at least one agent (A2) that is an inhibitor of a caspase family protease.

DETAILED DESCRIPTION - A method (M1) for modulating responsiveness to a corticosteroid in a subject, comprising selecting a subject in need of modulation of responsiveness to a corticosteroid and administering:

(a) an agent (A1) which antagonizes a target that regulates production of interferon-gamma (IFN-gamma) in the subject, the agent being administered at a dosage and by a route sufficient to inhibit production of IFN-gamma; or

(b) at least one agent (A2) that is an inhibitor of a caspase family protease; and

(c) a corticosteroid.

The responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

An INDEPENDENT CLAIM is also given for a method (M2) for regulating the production of IFN-gamma in a subject, comprising administering a corticosteroid and an agent which antagonizes a target that regulates production of IFN-gamma such that production of IFN-gamma is modulated in the subject.

ACTIVITY - Immunosuppressive; antiinflammatory; dermatological; antibacterial; cytostatic; antiasthmatic; anticonvulsant; antidiabetic; antiarthritic; antirheumatic; neuroprotective; antiallergic; antiulcer; ophthalmological; antianemic.

Interleukin converting enzyme (ICE)-deficient and wild type mice first were sensitized with Propionibacterium acnes cell wall material (1 mg per mouse) to induce low grade inflammation and six days later were challenged with lipopolysaccharide (LPS) (1 microgram per mouse in 0.1 ml of saline intravenously). Thirty minutes after LPS administration, the mice were treated with the corticosteroid dexamethasone (4 mg/kg per mouse in 0.5 ml 95% saline/0.5% ethanol, intraperitoneally). Control mice were treated with vehicle alone. All mice were bled 90 minutes after LPS administration and the serum samples were analyzed for the presence of tumor necrosis alpha (TNF-alpha) by standard ELISA (Enzyme linked immunosorbant assay).

Wild type and ICE deficient mice treated with vehicle alone had similar levels of serum TNF-alpha. Treatment of wild type mice with dexamethasone did not significantly affect serum TNF-alpha levels, demonstrating their resistance to steroid treatment in this septic shock model. In contrast, treatment of the ICE deficient mice with dexamethasone suppressed serum TNF-alpha levels by 74% (p less than 0.002). These data indicate that inhibition of ICE activity reverses resistance to steroid treatment in a septic shock model.

MECHANISM OF ACTION - **IL-12 antagonist**; IL-18 antagonist; phosphodiesterase IV inhibitor; a beta-2 agonist; a STAT4 inhibitor; an anti-IL-1-alpha **antibody**; an anti-IL-1-beta **antibody**; an anti-tumor necrosis factor **antibody**; a natural killer cell antagonist; a T-cell antagonist; caspase family protease inhibitor; gene therapy.

USE - The method is useful for treating a subject suffering from an autoimmune disease or disorder, an acute (e.g. infectious meningitis) or chronic (e.g. systemic lupus erythematosus or psoriasis) inflammatory disorder, septic shock or sepsis, graft versus host disease or transplant rejection, complications associated with post-surgical stress, Still's disease, leukemia or an immuno-inflammatory disease or disorder. The immuno-inflammatory disease or disorder is asthma, adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, multiple sclerosis, insulin-dependent diabetes mellitus, autoimmune arthritis, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy, primary biliary cirrhosis, uveitis posterior or interstitial lung fibrosis (claimed).

The method is useful for modulating corticosteroid responsiveness in a variety of clinical settings, for e.g. reversing steroid resistance, increasing steroid sensitivity, ameliorating a steroid rebound effect associated with administration of reduced dosages of the corticosteroid, or modulating corticosteroid activity, such that the corticosteroids can be tapered to zero (claimed).

Dwg.0/12

L15 ANSWER 6 OF 16 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-244560 [25] WPIDS
DNC C2001-073385
TI Composition comprising interleukin-12 p40 and IL-B30 polypeptide or its segment, useful for ameliorating **rheumatoid arthritis**, osteoarthritis, atherosclerosis, multiple sclerosis, vasculitis and tumor.
DC B04 D16
IN DE WAAL MALEFYT, R; KASTELEIN, R A; LIRA, S A; NARULA, S K; OPPMANN, B; RENNICK, D M; WIEKOWSKI, M T
PA (SCHE) SCHERING CORP
CYC 92
PI WO 2001018051 A2 20010315 (200125)* EN 69p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CZ DE DK DM DZ EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX MZ NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA
AU 2000073608 A 20010410 (200137)
EP 1210434 A2 20020605 (200238) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2002034185 A 20020508 (200271)
ADT WO 2001018051 A2 WO 2000-US24686 20000908; AU 2000073608 A AU 2000-73608

20000908; EP 1210434 A2 EP 2000-961688 20000908, WO 2000-US24686 20000908; KR 2002034185 A KR 2002-703089 20020308

FDT AU 2000073608 A Based on WO 200118051; EP 1210434 A2 Based on WO 200118051

PRAI US 1999-164616P 19991110; US 1999-393090 19990909

AB WO 200118051 A UPAB: 20010508

NOVELTY - A composition (I) comprising a substantially pure polypeptide comprising a number of distinct segments of at least 7 contiguous amino acids from interleukin (IL)-12 p40 and/or IL-B30, and a substantially pure polypeptide comprising a segment of at least 11 contiguous amino acids from IL-12 p40 and/or IL-B30.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated or recombinant nucleic acid (II) encoding (I);

(2) a cell (III) comprising (II);

(3) a nucleic acid (IV) which hybridizes under wash conditions of 30 minutes at 50 deg. C and less than 1M salt to the natural mature coding portion of primate IL-12 p40 and IL-B30;

(4) an antagonist (V) of IL-12 p40/IL-B30 combined with a tumor necrosis factor-alpha (TNF alpha) antagonist, an **IL-12 antagonist**, IL-10, or steroids;

(5) a binding compound (VI) comprising an antigen binding site from an **antibody**, which specifically binds to (I) and comprising a substantially pure polypeptide comprising IL-12 p40 and IL-B30 polypeptide, or a polypeptide comprising IL-12 p40 fused to IL-B30, but not to either IL-12 p40 or IL-B30 polypeptide;

(6) a kit (VII) comprising:

(a) (I), and a compartment comprising the polypeptide, or instructions for use or disposal of reagents in the kit;

(b) (II), and a compartment comprising (II), a compartment further comprising a primate IL-12 p40 or IL-B30, or instructions for use or disposal of reagents in the kit or (VI); and

(c) a compartment comprising (VI), or instructions for use or disposal of reagents in the kit;

(7) producing (M1) an antigen:**antibody** complex, involves contacting, under appropriate conditions, a primate IL-12 p40/IL-B30 composition with (VI), allowing the complex to form;

(8) a composition (VIII) comprising (VI) which is sterile, or (VI) and a carrier such as an aqueous compound, including water, saline, and/or buffer;

(9) increasing (M2) the secretion of a primate IL-B30 involves expressing the polypeptide with IL-12 p40 or increasing the secretion of a primate IL-12 p40 involves expressing the IL-12 p40 with IL-B30; and

(10) screening (M3) for a receptor which binds (I) involves contacting the complex to a cell expressing the receptor under conditions allowing the complex to bind to the receptor, forming a detectable interaction.

ACTIVITY - Antirheumatic; antiarthritic; osteopathic; antiarthritic; neuroprotective; antiarteriosclerotic; cerebroprotective; vasotropic; cytostatic; antitumor; immunosuppressive.

MECHANISM OF ACTION - Modulator of physiology or development of cell in host; inducer of memory T-cell proliferation (claimed); modulator of trafficking or activation of leukocyte.

No supporting data is given.

USE - (I) is useful for modulating physiology or development of a cell or tissue in a host organism by contacting the cell with (I) or (V), resulting in an increased or decreased production of Interferon-gamma (IFN gamma), an enhanced Th1 response such as anti-tumor effect, adjuvant effect, anti-viral effect or antagonized allergic effect, and amelioration of an autoimmune condition or a chronic inflammatory condition. The contacting is in combination with IL-18, IL-12, radiation therapy or chemotherapy, an immune adjuvant or an anti-viral therapeutic. The antagonist is an **antibody** against IL-12 receptor subunit beta 1. The antagonist or agonist of mammalian IL-B30 protein is useful for

modulating the inflammatory response in an animal, by contacting cells in the animal with the agonist or antagonist, where the animal exhibits signs or symptoms of an acute phase inflammatory response in skin, lung, gastrointestinal, or liver tissue. The modulation is accelerating maturation of neutrophils into platelets and has an effect on immunoglobin A and G (IgA and IgG) . The antagonist is an **antibody** which binds to the mammalian IL-B30 or blocks signaling mediated by mammalian IL-B30. The antagonist or agonist is administered in combination with an anti-inflammatory cytokine agonist or antagonist, an analgesic, an anti-inflammatory agent, or a steriod. IL-B30 or its agonist is useful inducing the proliferation of memory T-cells (all claimed).

Agonist or antagonist of IL-B30 protein is useful for modulating the trafficking or activation of a leukocyte in an animal experiencing science or symptoms of autoimmunity, an inflammatory condition, tissue specific autoimmunity, degenerative autoimmunity, **rheumatoid arthritis**, osteoarthritis, atherosclerosis, multiple sclerosis, vasculitis, delayed hypersensitivities, skin grafting, a transplant, spinal injury, stroke, neurodegeneration, an infectious disease, ischemia, cancer, tumors, multiple myeloma, Castleman's disease, postmenopausal osteoporosis or IL-6-associated diseases.

IL-12 p40/IL-B30 is useful as an immunogen for the production a antisera or **antibodies** specific for binding. (I) is useful for in vitro assays, scientific research, and the synthesis or manufacture of nucleic acids or **antibodies**. (II) is useful in forensic science. Dwg.0/0

L15 ANSWER 7 OF 16 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2001-08257 BIOTECHDS
TI Composition containing interleukin-12 p40 and IL-B30 protein or its segment, useful for ameliorating **rheumatoid arthritis** , osteoarthritis, atherosclerosis, multiple sclerosis, vasculitis and tumor;
vector-mediated gene transfer and expression in host cell, **antibody** and antagonist
AU Oppmann B; De Waal Malefyt R; Rennick D M; Kastelein R A; Wiekowski M T; Lira S A; Narula S K
PA Schering-USA
LO Kenilworth, NJ, USA.
PI WO 2001018051 15 Mar 2001
AI WO 2000-US24686 8 Sep 2000
PRAI US 1999-164616 10 Nov 1999; US 1999-393090 9 Sep 1999
DT Patent
LA English
OS WPI: 2001-244560 [25]
AB A composition containing a substantially pure protein containing a number of distinct segments of at least 7 contiguous amino acids from interleukin (IL)-12 p40 and/or IL-B30, and a substantially pure protein containing a segment of at least 11 contiguous amino acids from IL-12 p40 and/or IL-B30, is new. Also claimed are: a recombinant nucleic acid encoding the protein; a cell containing the nucleic acid; a nucleic acid which hybridizes under wash conditions of 30 min at 50 deg and less than 1M salt to the natural mature coding portion of primate IL-12 p40 and IL-B30; an antagonist of IL-12 p40/IL-B30 combined with a tumor necrosis factor-alpha (TNF-alpha) antagonist, an **IL-12 antagonist**, IL-10 or steroids; a binding compound containing an antigen binding site from an **antibody** which specifically binds to the protein; a kit containing the composition, polynucleotide and a binding compound; producing an antigen:**antibody** complex; a composition containing a binding compound; increasing the secretion of a primate IL-B30; and screening for a receptor which binds the composition. The composition is useful for modulating physiology or development of a cell or tissue0. (69pp)

L15 ANSWER 8 OF 16 USPATFULL
AN 2001:63494 USPATFULL
TI **Antibodies** against human IL-12
IN Gately, Maurice Kent, Parsippany, NJ, United States
Presky, David Howard, Glen Ridge, NJ, United States
PA Hoffman-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 6225117 B1 20010501
AI US 1999-232522 19990119 (9)
PRAI US 1998-72333P 19980123 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: DiBrino, Marianne
LREP Johnston, George W., Rocha-Tramaloni, Patricia S., Silverman, Robert A.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1122
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel p75 heterodimer specific anti-human IL-12 **antibodies** that are characterized by a higher potency and greater efficacy in neutralizing human IL-12 bioactivity than known heterodimer specific IL-12 monoclonal **antibodies**. The heterodimer specific **antibodies** recognize one or more epitopes of the human IL-12 p75 heterodimer, but do not bind to the p40 subunit alone. The heterodimer specific IL-12 **antibodies** neutralize rhesus monkey IL-12 bioactivity with a potency similar to their potency for neutralizing human IL-12 bioactivity making them useful **IL-12 antagonists** for in vivo studies in the rhesus monkey.

L15 ANSWER 9 OF 16 USPATFULL
AN 2000:50737 USPATFULL
TI Methods and compositions for modulating responsiveness to corticosteroids
IN Sekut, Les, Westborough, MA, United States
Carter, Adam, Newburyport, MA, United States
Ghayur, Tariq, Grafton, MA, United States
Banerjee, Subhashis, Shrewsbury, MA, United States
Tracey, Daniel E., Harvard, MA, United States
PA BASF Aktiengesellschaft, Rheinland Pfalz, Germany, Federal Republic of (non-U.S. corporation)
PI US 6054487 20000425
AI US 1997-820692 19970318 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Lahive & Cockfield, LLP
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method for modulating responsiveness to corticosteroids in a subject are provided. In the method of the invention, an agent which antagonizes a factor that regulates production of IFN-.gamma. in the subject is administered to the subject in combination with a corticosteroid such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject. In one embodiment, the agent is an interferon-.gamma. inducing factor (IGIF) antagonist. In another embodiment, the agent is an interleukin-12 (**IL-12**) **antagonist**. In a preferred embodiment, the agent is an inhibitor of a caspase family protease,

preferably an ICE inhibitor. In another preferred embodiment, the agent is an anti-IL-12 monoclonal **antibody**. Other preferred agents include phosphodiesterase IV inhibitors and beta-2 agonists. The methods of the invention can be used in the treatment of a variety of inflammatory and immunological diseases and disorders. Pharmaceutical compositions comprising an agent which antagonizes a factor that regulates production of IFN-.gamma. in a subject, a corticosteroid and a pharmaceutically acceptable carrier are also provided. A preferred composition comprises an ICE inhibitor, a corticosteroid and a pharmaceutically acceptable carrier.

L15 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS
AN 1999:487326 CAPLUS
DN 131:129052
TI **Antibodies** against human IL-12
IN Gately, Maurcie Kent; Presky, David Howard
PA F.Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9937682	A2	19990729	WO 1999-EP202	19990115
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9925177	A1	19990115	AU 1999-25177	19990115
	CA 2318052	AA	19990729	CA 1999-2318052	19990115
	BR 9907743	A	20001017	BR 1999-7743	19990115
	EP 1049717	A2	20001108	EP 1999-904780	19990115
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2002501085	T2	20020115	JP 2000-528602	19990115
	US 6225117	B1	20010501	US 1999-232522	19990119
	ZA 9900452	A	19990723	ZA 1999-452	19990121
PRAI	US 1998-72333P	P	19980123		
	WO 1999-EP202	W	19990115		

AB The present invention relates to p75 heterodimer specific anti-human IL-12 **antibodies** that are characterized by a higher potency and greater efficacy in neutralizing human IL-12 bioactivity than known heterodimer specific IL-12 monoclonal **antibodies**. The heterodimer specific **antibodies** recognize one or more epitopes of the human IL-12 p75 heterodimer, but do not bind to the p40 subunit alone. The heterodimer specific IL-12 **antibodies** neutralize rhesus monkey IL-12 bioactivity with a potency similar to their potency for neutralizing human IL-12 bioactivity making them useful **IL-12 antagonists**. The monoclonal **antibodies** are therefore useful for diseases assocd. with aberrant Th1-type helper cell activity, e.g. multiple sclerosis, **rheumatoid arthritis**, autoimmune diabetes mellitus, Crohn's disease and ulcerative colitis.

L15 ANSWER 11 OF 16 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 2
AN 1998-520957 [44] WPIDS
DNC C1998-156445
TI Modulating responsiveness to corticosteroid e.g. in treating auto-immune diseases - by administering agent antagonising target that regulates production of interferon gamma.

DC B01 B04 B05
IN BANERJEE, S; CARTER, A; GHAYUR, T; SEKUT, L; TRACEY, D E
PA (BADI) BASF AG
CYC 81
PI WO 9841232 A2 19980924 (199844)* EN 112p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9867604 A 19981012 (199907)
NO 9904506 A 19991117 (200005)
CZ 9903127 A3 20000315 (200021)
EP 998300 A1 20000510 (200027) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
US 6054487 A 20000425 (200027)
ES 2146192 T1 20000801 (200040)
BR 9810409 A 20000822 (200050)
CN 1269722 A 20001011 (200103)
SK 9901221 A3 20001211 (200103)
MX 9908433 A1 19991201 (200110)
KR 2000076420 A 20001226 (200134)
AU 734756 B 20010621 (200141)
JP 2002504091 W 20020205 (200212) 154p
HU 2001004439 A2 20020429 (200238)
NZ 337769 A 20020927 (200272)
ADT WO 9841232 A2 WO 1998-US4916 19980312; AU 9867604 A AU 1998-67604 19980312; NO 9904506 A WO 1998-US4916 19980312, NO 1999-4506 19990917; CZ 9903127 A3 WO 1998-US4916 19980312, CZ 1999-3127 19980312; EP 998300 A1 EP 1998-912929 19980312, WO 1998-US4916 19980312; US 6054487 A US 1997-820692 19970318; ES 2146192 T1 EP 1998-912929 19980312; BR 9810409 A BR 1998-10409 19980312, WO 1998-US4916 19980312; CN 1269722 A CN 1998-805124 19980312; SK 9901221 A3 WO 1998-US4916 19980312, SK 1999-1221 19980312; MX 9908433 A1 MX 1999-8433 19990914; KR 2000076420 A WO 1998-US4916 19980312, KR 1999-708524 19990918; AU 734756 B AU 1998-67604 19980312; JP 2002504091 W JP 1998-540633 19980312, WO 1998-US4916 19980312; HU 2001004439 A2 WO 1998-US4916 19980312, HU 2001-4439 19980312; NZ 337769 A NZ 1998-337769 19980312, WO 1998-US4916 19980312
FDT AU 9867604 A Based on WO 9841232; CZ 9903127 A3 Based on WO 9841232; EP 998300 A1 Based on WO 9841232; ES 2146192 T1 Based on EP 998300; BR 9810409 A Based on WO 9841232; KR 2000076420 A Based on WO 9841232; AU 734756 B Previous Publ. AU 9867604, Based on WO 9841232; JP 2002504091 W Based on WO 9841232; HU 2001004439 A2 Based on WO 9841232; NZ 337769 A Based on WO 9841232
PRAI US 1998-16346 19980130; US 1997-820692 19970318
AB WO 9841232 A UPAB: 19981104
Modulating responsiveness to corticosteroids comprises administering: (a) an agent which antagonises a target that regulates production of interferon- gamma (IFN- gamma), to inhibit production of IFN- gamma and (b) a corticosteroid.

Preferably, the agent which antagonises a target that regulates production of IFN- gamma is an IL-18 antagonist e.g. an inhibitor of a caspase family protease (especially an ICE inhibitor) or an **antibody** (fragment) or engineered binding protein that binds IL-18 or an IL-18 receptor. The agent may also be an **IL-12 antagonist** e.g. an agent that stimulates cyclic AMP production in cells that produce IL-12, especially a phosphodiesterase IV inhibitor such as a 4-arylpyrrolidinone, rolipram, denbufylline, tibenelast, nitraquazone, CP-80633, CP-77059 or a quinazolinedione or a beta -2 agonist such as salmeterol, fenoterol or isoproterenol.

USE- The process is used for treating septic shock, Crohn's disease, asthma, graft versus host disease or transplant rejection autoimmune

disease or disorder and immunoinflammatory diseases or disorders comprising adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, ulcerative colitis, multiple sclerosis, insulin dependent diabetes mellitus, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's syndrome, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anaemia, pure red cell anaemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy,primary biliary cirrhosis, uveitis posterior and interstitial lung fibrosis. Administration is oral, intravenous or ophthalmic.

ADVANTAGE - The process reverses steroid resistance and increases steroid sensitivity.

Dwg.0/0

L15 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS
AN 1998:351787 CAPLUS
DN 129:40158
TI Suppression of TNF.alpha. and IL-12 in therapy
IN Feldmann, Marc; Malfait, Anne-Marie Aline Michel; Butler, Debra Maree; Brennan, Fionula Mary; Maini, Ravinder Nath
PA Kennedy Institute of Rheumatology, UK; Feldmann, Marc; Malfait, Anne-Marie Aline Michel; Butler, Debra Maree; Brennan, Fionula Mary; Maini, Ravinder Nath
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9822137	A1	19980528	WO 1997-GB3151	19971117
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9749599	A1	19980610	AU 1997-49599	19971117
	EP 936923	A1	19990825	EP 1997-912367	19971117
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-749979 19961115
WO 1997-GB3151 19971117

AB Methods for treating and/or preventing a TNF.alpha.-mediated disease in an individual are disclosed. Also disclosed are compns. comprising a TNF antagonist and an **IL-12 antagonist**. The TNF.alpha. antagonist is an **antibody** or a TNF receptor/IgG fusion protein or thalidomide, and the **IL-12 antagonist** is an **antibody** or phosphodiesterase inhibitor, e.g. pentoxifylline or rolipram. TNF.alpha.-mediated diseases include **rheumatoid arthritis**, Crohn's disease, and acute and chronic immune diseases assocd. with transplantation.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 16 USPATFULL
AN 1998:161997 USPATFULL
TI **Antibody** to interleukin-12 receptor
IN Gately, Maurice Kent, Pine Brook, NJ, United States
Presky, David Howard, Glen Ridge, NJ, United States
Wu, Chang-you, Belleville, NJ, United States
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5853721 19981229
AI US 1995-381059 19950131 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Sun-Hoffman, Lin
LREP Johnston, George W., Tramaloni, Dennis P., Kass, Alan P.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 33 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 1418
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel **antibody** against the IL-12 receptor and a novel combination of anibodies anainst the IL-12 receptor. The novel anti-IL-12 receptor anbody, designated as 2B10, provided in accordance with the present invention binds to the human IL-12 receptor but which is not capable of inhibiting the binding of human IL-12 to the high affinity human IL-12 receptor and is not capable of neutralizing human IL-12 bioactivity by binding to human IL-12 receptor.

L15 ANSWER 14 OF 16 USPATFULL
AN 1998:135151 USPATFULL
TI Human receptor for interleukin-12
IN Chua, Anne On, Wayne, NJ, United States
Gubler, Ulrich Andreas, Glen Ridge, NJ, United States
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5831007 19981103
AI US 1995-419652 19950411 (8)
RLI Division of Ser. No. US 1994-248532, filed on 31 May 1994, now patented, Pat. No. US 5536657 which is a continuation-in-part of Ser. No. US 1993-94713, filed on 19 Jul 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Johnston, George W., Epstein, William H., Bucholz, Briana C.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 26 Drawing Page(s)
LN.CNT 1937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to substantially pure Interleukin-12 receptor cDNAs and protein and uses therefore. The Interleukin-12 receptor is shown to be a member of the cytokine receptor superfamily and has a high homology to human gp130.

L15 ANSWER 15 OF 16 USPATFULL
AN 96:63048 USPATFULL
TI Recombinant DNA encoding human receptor for interleukin-12
IN Chua, Anne O., Wayne, NJ, United States
Gubler, Ulrich A., Glen Ridge, NJ, United States
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5536657 19960716
AI US 1994-248532 19940531 (8)
RLI Continuation-in-part of Ser. No. US 1993-94713, filed on 19 Jul 1993, now abandoned

DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Gould, George M., Johnston, George W., Kass, Alan P.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 34 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 1755
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to substantially pure Interleukin-12 receptor cDNAs and protein and uses therefore. The Interleukin-12 receptor is shown to be a member of the cytokine receptor superfamily and has a high homology to human gp130.

L15 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS
AN 1995:934127 CAPLUS
DN 123:337469
TI Use of IL-12 and **IL-12 antagonists** in treatment of autoimmune diseases
IN Leonard, John P.; Goldman, Samuel; O'Hara, Richard, Jr.
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524918	A1	19950921	WO 1995-US2550	19950307
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9500960	A	19951010	ZA 1995-960	19950207
	TW 400233	B	20000801	TW 1995-84101380	19950214
	IL 112677	A1	20000131	IL 1995-112677	19950216
	CA 2185565	AA	19950921	CA 1995-2185565	19950307
	AU 9519749	A1	19951003	AU 1995-19749	19950307
	AU 689236	B2	19980326		
	EP 750509	A1	19970102	EP 1995-912666	19950307
	EP 750509	B1	20020515		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510444	T2	19971021	JP 1995-524044	19950307
	EP 1179348	A2	20020213	EP 2001-117762	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 217533	E	20020615	AT 1995-912666	19950307
	ES 2173953	T3	20021101	ES 1995-912666	19950307
	US 6338848	B1	20020115	US 2000-513380	20000225
PRAI	US 1994-212629	A	19940314		
	EP 1995-912666	A3	19950307		
	WO 1995-US2550	W	19950307		
	US 1995-560943	B1	19951120		

AB Autoimmune conditions such as multiple sclerosis, systemic lupus erythematosus, **rheumatoid arthritis**, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin-dependent diabetes mellitus, and autoimmune inflammatory eye disease, esp. conditions which are promoted by an increase in levels of IFN-.gamma. or TNF-.alpha., are treated in mammals by administering IL-12 or an **IL-12 antagonist**. Thus, lymphocytes from mice immunized with myelin proteolipid protein, and restimulated with a synthetic peptide from this protein, were injected into naive mice. The injected mice developed exptl. allergic encephalomyelitis which was exacerbated by incubation of these lymphocytes with IL-12 during restimulation, and alleviated by injection of a polyclonal **antibody** to IL-12.

=> d clm 8

L15 ANSWER 8 OF 16 USPATFULL
CLM What is claimed is:

1. An **antibody** to the human IL-12 p75 heterodimer, said heterodimer consisting a p35 subunit and a p40 subunit, wherein said **antibody** (a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and (b) is produced from a hybridoma cell line obtained from a mouse which is deficient in the gene encoding said p35 subunit or the p40 subunit of IL-12, said hybridoma cell line being selected from the group consisting of ATCC designation HB-12446, HB-12447, HB-12448, and HB-12449, or a humanized **antibody**, thereof.

2. A monoclonal **antibody** to human IL-12, said human IL-12 consisting of a p35 subunit and a p40 subunit which form a p75 heterodimer, wherein said monoclonal **antibody** (a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with an epitope presented by said p40 subunit; (b) neutralizes at least about 90% of the bioactivity of human IL-12; and (c) is produced from a hybridoma cell line selected from the group consisting of ATCC designation Nos. HB-12446, HB-12447, HB-12448, and HB-12449, or a humanized **antibody**, thereof.

3. A hybridoma that is capable of producing a monoclonal **antibody** to human IL-12, said human IL-12 consisting of a p35 subunit and a p40 subunit which form a p75 heterodimer, wherein said **antibody** (a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and (b) is produced from a cell line obtained from a mouse deficient in a gene encoding said p35 subunit or said p40 subunit, said hybridoma cell line being selected from the group consisting of ATCC designation HB-12446, HB-12447, HB-12448, and HB-12449.

4. The **antibody** of claim 1, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12446, or a humanized **antibody**, thereof.

5. The **antibody** of claim 4, wherein the **antibody** is humanized.

6. The **antibody** of claim 1, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12447, or a humanized **antibody**, thereof.

7. The **antibody** of claim 6, wherein the **antibody** is humanized.

8. The **antibody** of claim 1, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12448, or a humanized **antibody**, thereof.

9. The **antibody** of claim 8, wherein the **antibody** is humanized.

10. The **antibody** of claim 1, wherein the **antibody** produced by a hybridoma having ATCC designation number HB-12449, or a humanized **antibody**, thereof.

11. The **antibody** of claim 10, wherein the **antibody** is humanized.

12. The **antibody** of claim 2, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12446, or a humanized **antibody**, thereof.

13. The **antibody** of claim 12, wherein the **antibody** is humanized.

14. The **antibody** of claim 2, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12447, or a humanized **antibody**, thereof.

15. The **antibody** of claim 14, wherein the **antibody** is humanized.

16. The **antibody** of claim 2, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12448, or a humanized **antibody**, thereof.

17. The **antibody** of claim 16, wherein the **antibody** is humanized.

18. The **antibody** of claim 2, wherein the **antibody** is produced by a hybridoma having ATCC designation number HB-12449, or a humanized **antibody**, thereof.

19. The **antibody** of claim 18, wherein the **antibody** is humanized.

20. The hybridoma of claim 3 wherein the hybridoma is HIL-12F3-5F2 having ATCC designation number HB-12446.

21. The hybridoma of claim 3 wherein the hybridoma is HIL-12F3-16F2 having ATCC designation number HB-12447.

22. The hybridoma of claim 3, wherein the hybridoma is HIL-12F3-20E11 having ATCC designation number HB-12448.

23. The hybridoma of claim 3, wherein the hybridoma is HIL-12F3-16G2 having ATCC designation number HB-12449.

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=> d his

     (FILE 'HOME' ENTERED AT 12:47:48 ON 06 JAN 2003)

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 12:48:32 ON 06 JAN 2003
                E LEONARD JON P/AU
                E LEONARD JOHN P/AU
L1           120 S E3-E5
                E GOLDMAN SAMUEL/AU
L2            14 S E3
                E GOLDMAN S/AU
L3          1469 S E3
                E OHARA RICHARD/AU
                E OHARA RICHARD/AU
                E OHARA R/AU
L4            71 S E3
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L5          1672 S L1-L4
L6             0 S L5 AND RHEMUATOID ARTHRITIS
L7            15 S L5 AND RHEUMATOID ARTHRITIS
L8             5 S L7 AND IL-12
L9             3 S L7 AND IL-12 (5A) ANTAGONIST
L10            4 DUP REM L8 (1 DUPLICATE REMOVED)
L11       189113 S RHEUMATOID ARTHRITIS
L12          126 S IL-12 ANTAGONIST?
L13           49 S L12 AND ANTIBOD?
L14           18 S L11 AND L13
L15           16 DUP REM L14 (2 DUPLICATES REMOVED)

=> s l11 and (prednisone or steroid or combination therapy)
L16       11436 L11 AND (PREDNISONE OR STEROID OR COMBINATION THERAPY)

=> s l16 and l12
L17           7 L16 AND L12

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18           5 DUP REM L17 (2 DUPLICATES REMOVED)

=> d bib ab 1-5

L18  ANSWER 1 OF 5  USPATFULL
AN      2002:48631  USPATFULL
TI      THERAPEUTIC COMPOUNDS FOR INHIBITING INTERLEUKIN-12 SIGNALING AND
        METHODS FOR USING SAME
IN      KLEIN, J. PETER, VASHON, WA, UNITED STATES
        KLAUS, STEPHEN J., SEATTLE, WA, UNITED STATES
        KUMAR, ANIL M., MERCER ISLAND, WA, UNITED STATES
        GONG, BAOQING, SHORELINE, WA, UNITED STATES
PI      US 2002028823      A1   20020307
AI      US 1999-288556     A1   19990409 (9)
RLI     Continuation-in-part of Ser. No. US 1998-8020, filed on 16 Jan 1998,
        ABANDONED
DT      Utility
FS      APPLICATION
LREP    MCDERMOTT WILL & EMERY, 600 13TH STREET, N.W., WASHINGTON, DC,
        20005-3096
CLMN    Number of Claims: 20
ECL     Exemplary Claim: 1
DRWN    1 Drawing Page(s)
LN.CNT 4381
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      Novel heterocyclic compounds having a six membered ring structure fused
        to a five membered ring structure are found to be useful for the
        treatment and prevention of symptoms or manifestations associated with
        disorders affected by Interleukin-12 ("IL-12") intracellular signaling,
        such as, for example, Th1 cell-mediated disorders. The therapeutic
        compounds, pharmaceutically acceptable derivatives (e.g., resolved
        enantiomers, diastereomers, tautomers, salts and solvates thereof) or
        prodrugs thereof, have the following general formula:   ##STR1##

        Each X, Y and Z are independently selected from a member of the group
        consisting of C(R.sub.3), N, N(R.sub.3) and S. Each R.sub.1, R.sub.2 and
        R.sub.3 is substituted or unsubstituted and is independently selected
        from a member of the group consisting of hydrogen, halo, oxo,
        C.sub.(1-20)alkyl, C.sub.(1-20)hydroxyalkyl, C.sub.(1-20)thioalkyl,
        C.sub.(1-20)alkylamino, C.sub.(1-20)alkylaminoalkyl,
        C.sub.(1-20)aminoalkyl, C.sub.(1-20)aminoalkoxyalkenyl,
        C.sub.(1-20)aminoalkoxyalkynyl, C.sub.(1-20)diaminoalkyl,
        C.sub.(1-20)triaminoalkyl, C.sub.(1-20)tetraaminoalkyl,
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C.sub.(5-15)aminotrialkoxyamino, C.sub.(1-20)alkylamido, C.sub.(1-20)alkylamidoalkyl, C.sub.(1-20)amidoalkyl, C.sub.(1-20)acetamidoalkyl, C.sub.(1-20)alkenyl, C.sub.(1-20)alkynyl, C.sub.(3-8)alkoxyl, C.sub.(1-11)alkoxyalkyl, and C.sub.(1-20)dialkoxyalkyl.

L18 ANSWER 2 OF 5 USPATFULL
AN 2002:276097 USPATFULL
TI Method of inhibiting interleukin-12 signaling
IN Klaus, Stephen J., Seattle, WA, United States
Klein, J. Peter, Vashon Island, WA, United States
Kumar, Anil M., Mercer Island, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6469017 B1 20021022
AI US 1998-8020 19980116 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Criares, Theodore J.
LREP Foley & Lardner
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 898
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for blocking IL-12 signaling by administration of the following compound: ##STR1##

wherein, R.sub.1 is H, CH.sub.3, sulfate, phosphate, or salt thereof; R.sub.2 is alkyl (C.sub.1-12), alkoxyalkyl (C.sub.1-11), dialkoxyalkyl, CH.sub.2C.sub.6H.sub.5, --CH.sub.2-furan, biotin; and R.sub.3 is H, CH.sub.3 or CH.sub.2C.sub.6H.sub.5.

L18 ANSWER 3 OF 5 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1
AN 2001-244697 [25] WPIDS
DNC C2001-073427
TI Modulating responsiveness to a corticosteroid by administering a corticosteroid with an agent which antagonizes a target that regulates interferon-gamma production or an caspase family protease inhibitor, useful for treating asthma.
DC B04 B05 D16
IN BANERJEE, S; CARTER, A; GHAYUR, T; SEKUT, L; TRACEY, D E
PA (BADI) BASF AG
CYC 94
PI WO 2001019373 A2 20010322 (200125)* EN 152p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000071276 A 20010417 (200140)
ADT WO 2001019373 A2 WO 2000-US24725 20000908; AU 2000071276 A AU 2000-71276 20000908
FDT AU 2000071276 A Based on WO 200119373
PRAI US 1999-398555 19990917
AB WO 200119373 A UPAB: 20010508
NOVELTY - A new method (M1) for modulating responsiveness to a corticosteroid in a subject comprises administering a corticosteroid with an agent (A1) which antagonizes a target that regulates production of interferon-gamma (IFN-gamma) or at least one agent (A2) that is an inhibitor of a caspase family protease.
DETAILED DESCRIPTION - A method (M1) for modulating responsiveness to a corticosteroid in a subject, comprising selecting a subject in need of

modulation of responsiveness to a corticosteroid and administering:

(a) an agent (A1) which antagonizes a target that regulates production of interferon-gamma (IFN-gamma) in the subject, the agent being administered at a dosage and by a route sufficient to inhibit production of IFN-gamma; or

(b) at least one agent (A2) that is an inhibitor of a caspase family protease; and

(c) a corticosteroid.

The responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

An INDEPENDENT CLAIM is also given for a method (M2) for regulating the production of IFN-gamma in a subject, comprising administering a corticosteroid and an agent which antagonizes a target that regulates production of IFN-gamma such that production of IFN-gamma is modulated in the subject.

ACTIVITY - Immunosuppressive; antiinflammatory; dermatological; antibacterial; cytostatic; antiasthmatic; anticonvulsant; antidiabetic; antiarthritic; antirheumatic; neuroprotective; antiallergic; antiulcer; ophthalmological; antianemic.

Interleukin converting enzyme (ICE)-deficient and wild type mice first were sensitized with Propionibacterium acnes cell wall material (1 mg per mouse) to induce low grade inflammation and six days later were challenged with lipopolysaccharide (LPS) (1 microgram per mouse in 0.1 ml of saline intravenously). Thirty minutes after LPS administration, the mice were treated with the corticosteroid dexamethasone (4 mg/kg per mouse in 0.5 ml 95% saline/0.5% ethanol, intraperitoneally). Control mice were treated with vehicle alone. All mice were bled 90 minutes after LPS administration and the serum samples were analyzed for the presence of tumor necrosis alpha (TNF-alpha) by standard ELISA (Enzyme linked immunosorbant assay).

Wild type and ICE deficient mice treated with vehicle alone had similar levels of serum TNF-alpha. Treatment of wild type mice with dexamethasone did not significantly affect serum TNF-alpha levels, demonstrating their resistance to **steroid** treatment in this septic shock model. In contrast, treatment of the ICE deficient mice with dexamethasone suppressed serum TNF-alpha levels by 74% (p less than 0.002). These data indicate that inhibition of ICE activity reverses resistance to **steroid** treatment in a septic shock model.

MECHANISM OF ACTION - **IL-12 antagonist**; IL-18 antagonist; phosphodiesterase IV inhibitor; a beta-2 agonist; a STAT4 inhibitor; an anti-IL-1-alpha antibody; an anti-IL-1-beta antibody; an anti-tumor necrosis factor antibody; a natural killer cell antagonist; a T-cell antagonist; caspase family protease inhibitor; gene therapy.

USE - The method is useful for treating a subject suffering from an autoimmune disease or disorder, an acute (e.g. infectious meningitis) or chronic (e.g. systemic lupus erythematosus or psoriasis) inflammatory disorder, septic shock or sepsis, graft versus host disease or transplant rejection, complications associated with post-surgical stress, Still's disease, leukemia or an immuno-inflammatory disease or disorder. The immuno-inflammatory disease or disorder is asthma, adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, multiple sclerosis, insulin-dependent diabetes mellitus, autoimmune arthritis, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum

leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy, primary biliary cirrhosis, uveitis posterior or interstitial lung fibrosis (claimed).

The method is useful for modulating corticosteroid responsiveness in a variety of clinical settings, for e.g. reversing **steroid** resistance, increasing **steroid** sensitivity, ameliorating a **steroid** rebound effect associated with administration of reduced dosages of the corticosteroid, or modulating corticosteroid activity, such that the corticosteroids can be tapered to zero (claimed). Dwg.0/12

L18 ANSWER 4 OF 5 USPATFULL
AN 2000:50737 USPATFULL
TI Methods and compositions for modulating responsiveness to corticosteroids
IN Sekut, Les, Westborough, MA, United States
Carter, Adam, Newburyport, MA, United States
Ghayur, Tariq, Grafton, MA, United States
Banerjee, Subhashis, Shrewsbury, MA, United States
Tracey, Daniel E., Harvard, MA, United States
PA BASF Aktiengesellschaft, Rheinland Pfalz, Germany, Federal Republic of (non-U.S. corporation)
PI US 6054487 20000425
AI US 1997-820692 19970318 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Lahive & Cockfield, LLP
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method for modulating responsiveness to corticosteroids in a subject are provided. In the method of the invention, an agent which antagonizes a factor that regulates production of IFN-.gamma. in the subject is administered to the subject in combination with a corticosteroid such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject. In one embodiment, the agent is an interferon-.gamma. inducing factor (IGIF) antagonist. In another embodiment, the agent is an interleukin-12 (**IL-12**) **antagonist**. In a preferred embodiment, the agent is an inhibitor of a caspase family protease, preferably an ICE inhibitor. In another preferred embodiment, the agent is an anti-IL-12 monoclonal antibody. Other preferred agents include phosphodiesterase IV inhibitors and beta-2 agonists. The methods of the invention can be used in the treatment of a variety of inflammatory and immunological diseases and disorders. Pharmaceutical compositions comprising an agent which antagonizes a factor that regulates production of IFN-.gamma. in a subject, a corticosteroid and a pharmaceutically acceptable carrier are also provided. A preferred composition comprises an ICE inhibitor, a corticosteroid and a pharmaceutically acceptable carrier.

L18 ANSWER 5 OF 5 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 2
AN 1998-520957 [44] WPIDS
DNC C1998-156445
TI Modulating responsiveness to corticosteroid e.g. in treating auto-immune diseases - by administering agent antagonising target that regulates production of interferon gamma.
DC B01 B04 B05

IN BANERJEE, S; CARTER, A; GHAYUR, T; SEKUT, L; TRACEY, D E
PA (BADI) BASF AG
CYC 81
PI WO 9841232 A2 19980924 (199844)* EN 112p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9867604 A 19981012 (199907)
NO 9904506 A 19991117 (200005)
CZ 9903127 A3 20000315 (200021)
EP 998300 A1 20000510 (200027) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
US 6054487 A 20000425 (200027)
ES 2146192 T1 20000801 (200040)
BR 9810409 A 20000822 (200050)
CN 1269722 A 20001011 (200103)
SK 9901221 A3 20001211 (200103)
MX 9908433 A1 19991201 (200110)
KR 2000076420 A 20001226 (200134)
AU 734756 B 20010621 (200141)
JP 2002504091 W 20020205 (200212) 154p
HU 2001004439 A2 20020429 (200238)
NZ 337769 A 20020927 (200272)
ADT WO 9841232 A2 WO 1998-US4916 19980312; AU 9867604 A AU 1998-67604 19980312; NO 9904506 A WO 1998-US4916 19980312, NO 1999-4506 19990917; CZ 9903127 A3 WO 1998-US4916 19980312, CZ 1999-3127 19980312; EP 998300 A1 EP 1998-912929 19980312, WO 1998-US4916 19980312; US 6054487 A US 1997-820692 19970318; ES 2146192 T1 EP 1998-912929 19980312; BR 9810409 A BR 1998-10409 19980312, WO 1998-US4916 19980312; CN 1269722 A CN 1998-805124 19980312; SK 9901221 A3 WO 1998-US4916 19980312, SK 1999-1221 19980312; MX 9908433 A1 MX 1999-8433 19990914; KR 2000076420 A WO 1998-US4916 19980312, KR 1999-708524 19990918; AU 734756 B AU 1998-67604 19980312; JP 2002504091 W JP 1998-540633 19980312, WO 1998-US4916 19980312; HU 2001004439 A2 WO 1998-US4916 19980312, HU 2001-4439 19980312; NZ 337769 A NZ 1998-337769 19980312, WO 1998-US4916 19980312
FDT AU 9867604 A Based on WO 9841232; CZ 9903127 A3 Based on WO 9841232; EP 998300 A1 Based on WO 9841232; ES 2146192 T1 Based on EP 998300; BR 9810409 A Based on WO 9841232; KR 2000076420 A Based on WO 9841232; AU 734756 B Previous Publ. AU 9867604, Based on WO 9841232; JP 2002504091 W Based on WO 9841232; HU 2001004439 A2 Based on WO 9841232; NZ 337769 A Based on WO 9841232
PRAI US 1998-16346 19980130; US 1997-820692 19970318
AB WO 9841232 A UPAB: 19981104
Modulating responsiveness to corticosteroids comprises administering: (a) an agent which antagonises a target that regulates production of interferon- gamma (IFN- gamma), to inhibit production of IFN- gamma and (b) a corticosteroid.

Preferably, the agent which antagonises a target that regulates production of IFN- gamma is an IL-18 antagonist e.g. an inhibitor of a caspase family protease (especially an ICE inhibitor) or an antibody (fragment) or engineered binding protein that binds IL-18 or an IL-18 receptor. The agent may also be an **IL-12 antagonist** e.g. an agent that stimulates cyclic AMP production in cells that produce IL-12, especially a phosphodiesterase IV inhibitor such as a 4-arylpyrrolidinone, rolipram, denbufylline, tibenelast, nitraquazone, CP-80633, CP-77059 or a quinazolinedione or a beta -2 agonist such as salmeterol, fenoterol or isoproterenol.

USE- The process is used for treating septic shock, Crohn's disease, asthma, graft versus host disease or transplant rejection autoimmune disease or disorder and immunoinflammatory diseases or disorders

comprising adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, ulcerative colitis, multiple sclerosis, insulin dependent diabetes mellitus, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's syndrome, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anaemia, pure red cell anaemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy,primary biliary cirrhosis, uveitis posterior and interstitial lung fibrosis. Administration is oral, intravenous or ophthalmic.

ADVANTAGE - The process reverses **steroid** resistance and increases **steroid** sensitivity.

Dwg.0/0

=> d clm 2

L18 ANSWER 2 OF 5 USPATFULL

CLM What is claimed is:

1. A method of inhibiting Interleukin-12 signaling in a mammal having a CD4+ Th1 cell-mediated inflammatory response, the method comprising administering a signal inhibiting amount of a compound of the following formula: ##STR10## wherein, R.sub.1 is CH.sub.3, sulfate, phosphate, or salt thereof; R.sub.2 is alkyl (C.sub.1-12), alkoxyalkyl (C.sub.1-11), dialkoxyalkyl, CH.sub.2C.sub.6H.sub.5, --CH.sub.2-furan, biotin; and R.sub.3 is H, CH.sub.3 or CH.sub.2C.sub.6H.sub.5.

2. The method of claim 1, wherein R.sub.2 is alkyl (C.sub.1-12), CH.sub.2C.sub.6H.sub.5, --CH.sub.2-furan, or biotin and R.sub.3 is H or methyl.

3. The method of claim 2, wherein R.sub.2 is alkyl (C.sub.1-12), biotin or --CH.sub.2-furan.

4. The method of claim 3, wherein R.sub.1 is sulfate or phosphate or a salt thereof, and R.sub.2 and R.sub.3 are CH.sub.3.

5. The method of claim 1, wherein the compound is of the following formula: ##STR11##

6. The method of claim 1, wherein the compound is of the following formula: ##STR12##

7. A method of inhibiting Interleukin-12 signaling in a mammal having a CD4+ Th1 cell-mediated inflammatory response, the method comprising administering a signal inhibiting amount of a compound of the following formula: ##STR13## wherein, R.sub.1 is H, CH.sub.3, sulfate, phosphate, or salt thereof; R.sub.2 is alkyl (C.sub.1-12), alkoxyalkyl (C.sub.1-11), dialkoxyalkyl, CH.sub.2C.sub.6H.sub.5, --CH.sub.2-furan, biotin; and R.sub.3 is H, CH.sub.3 or CH.sub.2C.sub.6H.sub.5, provided that when R1 is H, R2 is not alkyl (C.sub.1-12) and R3 is not CH3.

8. The method of claim 7, wherein a disease condition, which exhibits The CD4+ Th1 cell-mediated inflammatory response, is selected from the group consisting of chronic inflammatory disease, chronic intestinal inflammation, arthritis, psoriasis, asthma, and autoimmune disorders.

9. The method of claim 7, wherein an autoimmune disorder generates the CD4+ Th1 cell-mediated inflammatory response.

10. The method of claim 9, wherein the autoimmune disorder is selected from the group consisting of type-1 insulin dependent diabetes mellitus ("IDDM"), multiple sclerosis, **rheumatoid arthritis**, inflammatory bowel disease, lupus disorders, and acute graft-versus-host disease.

11. The method of claim 7, wherein the mammal is a human.

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=> d his

     (FILE 'HOME' ENTERED AT 12:47:48 ON 06 JAN 2003)

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     LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 12:48:32 ON 06 JAN 2003
                E LEONARD JON P/AU
                E LEONARD JOHN P/AU
L1           120 S E3-E5
                E GOLDMAN SAMUEL/AU
L2            14 S E3
                E GOLDMAN S/AU
L3          1469 S E3
                E OHARA RICHARD/AU
                E OHARA RICHARD/AU
                E OHARA R/AU
L4            71 S E3
L5          1672 S L1-L4
L6             0 S L5 AND RHEMUATOID ARTHRITIS
L7            15 S L5 AND RHEUMATOID ARTHRITIS
L8             5 S L7 AND IL-12
L9             3 S L7 AND IL-12 (5A) ANTAGONIST
L10            4 DUP REM L8 (1 DUPLICATE REMOVED)
L11       189113 S RHEUMATOID ARTHRITIS
L12          126 S IL-12 ANTAGONIST?
L13           49 S L12 AND ANTIBOD?
L14           18 S L11 AND L13
L15           16 DUP REM L14 (2 DUPLICATES REMOVED)
L16        11436 S L11 AND (PREDNISONE OR STEROID OR COMBINATION THERAPY)
L17            7 S L16 AND L12
L18            5 DUP REM L17 (2 DUPLICATES REMOVED)

=> s l11 and combination therapy
L19        2190 L11 AND COMBINATION THERAPY

=> s l19 and l13
L20           0 L19 AND L13

=> s l19 and l12
L21           0 L19 AND L12

=> s l11 and prednisone
L22        4836 L11 AND PREDNISONE

=> s l22 and l12
L23           4 L22 AND L12

=> d bib 1-4

L23  ANSWER 1 OF 4  WPIDS (C) 2003 THOMSON DERWENT
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AN 2001-244697 [25] WPIDS
DNC C2001-073427
TI Modulating responsiveness to a corticosteroid by administering a corticosteroid with an agent which antagonizes a target that regulates interferon-gamma production or an caspase family protease inhibitor, useful for treating asthma.
DC B04 B05 D16
IN BANERJEE, S; CARTER, A; GHAYUR, T; SEKUT, L; TRACEY, D E
PA (BADI) BASF AG
CYC 94
PI WO 2001019373 A2 20010322 (200125)* EN 152p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000071276 A 20010417 (200140)
ADT WO 2001019373 A2 WO 2000-US24725 20000908; AU 2000071276 A AU 2000-71276 20000908
FDT AU 2000071276 A Based on WO 200119373
PRAI US 1999-398555 19990917

L23 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2001:208111 CAPLUS
DN 134:247241
TI Methods and compositions for modulating responsiveness to corticosteroids
IN Sekut, Les; Carter, Adam; Ghayur, Tariq; Banerjee, Subhashis; Tracey, Daniel E.
PA BASF A.-G., Germany
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001019373	A2	20010322	WO 2000-US24725	20000908
	WO 2001019373	A3	20011004		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-398555 A1 19990917

L23 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1998:640257 CAPLUS
DN 129:255530
TI Methods and compositions for modulating responsiveness to corticosteroids
IN Sekut, Les; Carter, Adam; Chayur, Tariq; Banerjee, Subhashis; Tracey, Daniel E.
PA Basf A.-G., Germany
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 9841232	A2	19980924	WO 1998-US4916	19980312
	WO 9841232	A3	20001005		
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6054487	A	20000425	US 1997-820692	19970318
	AU 9867604	A1	19981012	AU 1998-67604	19980312
	AU 734756	B2	20010621		
	EP 998300	A1	20000510	EP 1998-912929	19980312
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	BR 9810409	A	20000822	BR 1998-10409	19980312
	JP 2002504091	T2	20020205	JP 1998-540633	19980312
	NO 9904506	A	19991117	NO 1999-4506	19990917
PRAI	US 1997-820692	A2	19970318		
	US 1998-16346	A2	19980130		
	WO 1998-US4916	W	19980312		

L23 ANSWER 4 OF 4 USPATFULL
AN 2000:50737 USPATFULL
TI Methods and compositions for modulating responsiveness to corticosteroids
IN Sekut, Les, Westborough, MA, United States
Carter, Adam, Newburyport, MA, United States
Ghayur, Tariq, Grafton, MA, United States
Banerjee, Subhashis, Shrewsbury, MA, United States
Tracey, Daniel E., Harvard, MA, United States
PA BASF Aktiengesellschaft, Rheinland Pfalz, Germany, Federal Republic of (non-U.S. corporation)
PI US 6054487 20000425
AI US 1997-820692 19970318 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Lahive & Cockfield, LLP
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d clm 4

L23 ANSWER 4 OF 4 USPATFULL
CLM What is claimed is:

1. A method for modulating responsiveness to a corticosteroid in a subject, comprising administering to the subject suffering from a condition normally responsive to corticosteroid therapy: an interleukin-1 .beta. converting enzyme (ICE) inhibitor being administered at a dosage and by a route sufficient to inhibit production of IFN-.gamma. in the subject; and a corticosteroid, such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

2. The method of claim 1, wherein the ICE inhibitor is an IFN-.gamma. inducing factor (IGIF) antagonist, the ICE inhibitor being administered at a dosage and by a route sufficient to inhibit IGIF activity in the subject.

3. The method of claim 1, wherein the corticosteroid is selected from the group consisting of cortisone, hydrocortisone, beclomethasone, flunisolide, **prednisone**, prednisolone, methylprednisolone, triamcinolone, deflazacort, betamethasone and dexamethasone.

4. The method of claim 1, wherein the subject is suffering from septic shock.

5. The method of claim 1, wherein the subject is suffering from Crohn's disease.

6. The method of claim 1, wherein the subject is suffering from asthma.

7. The method of claim 1, wherein the subject is suffering from graft versus host disease or transplant rejection.

8. The method of claim 1, wherein the subject is suffering from an autoimmune disease or disorder.

9. The method of claim 1, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of asthma, adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, multiple sclerosis, insulin-dependent diabetes mellitus, autoimmune arthritis, **rheumatoid arthritis** , juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy, primary biliary cirrhosis, uveitis posterior and interstitial lung fibrosis.

10. The method of claim 1, wherein the subject is suffering from an acute inflammatory disorder.

11. The method of claim 1, wherein the subject is suffering from a chronic inflammatory disorder.

12. The method of claim 1, wherein the ICE inhibitor and corticosteroid are administered such that steroid resistance in the subject is reversed, as compared to when a corticosteroid alone is administered to the subject.

13. The method of claim 1, wherein the ICE inhibitor and corticosteroid are administered such that steroid sensitivity in the subject is increased, as compared to when a corticosteroid alone is administered to the subject.

14. The method of claim 1, wherein the ICE inhibitor and the corticosteroid are administered to the subject according to a schedule that reduces the dosage of the corticosteroid over time and e method ameliorates a steroid rebound effect associated with administration of reduced dosages of the corticosteroid.

15. A method for modulating responsiveness to corticosteroids in a subject, comprising administering to the subject suffering from a condition normally responsive to corticosteroid therapy, an interleukin-1 .beta. converting enzyme (ICE) inhibitor; and a corticosteroid, such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

16. The method of claim 15, wherein the corticosteroid is selected from the group consisting of cortisone, hydrocortisone, beclomethasone, flunisolide, **prednisone**, prednisolone, methylprednisolone, triamcinolone, deflazacort, betamethasone and dexamethasone.

17. The method of claim 15, wherein the subject is suffering from septic shock.

18. The method of claim 15, wherein the subject is suffering from Crohn's disease.

19. The method of claim 15, wherein the subject is suffering from asthma.

20. The method of claim 15, wherein the subject is suffering from graft versus host disease or transplant rejection.

21. The method of claim 15, wherein the subject is suffering from an autoimmune disease or disorder.

22. The method of claim 15, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of asthma, adult respiratory distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, multiple sclerosis, insulin-dependent diabetes mellitus, autoimmune arthritis, **rheumatoid arthritis** , juvenile **rheumatoid arthritis**, psoriatic arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic thrombocytopenic purpura, autoimmune meningitis, myasthenia gravis, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Graves ophthalmopathy, primary biliary cirrhosis, uveitis posterior and interstitial lung fibrosis.

23. The method of claim 15, wherein the subject is suffering from an acute inflammatory disorder.

24. The method of claim 15, wherein the subject is suffering from a chronic inflammatory disorder.

25. The method of claim 24, wherein the ICE inhibitor and the corticosteroid are administered such that steroid resistance in the subject is reversed, as compared to when a corticosteroid alone is administered to the subject.

26. The method of claim 24, wherein the ICE inhibitor and the

corticosteroid are administered such that steroid sensitivity in the subject is increased, as compared to when a corticosteroid alone is administered to the subject.

27. The method of claim 24, wherein the ICE inhibitor and the corticosteroid are administered to the subject according to a schedule that reduces the dosage of the corticosteroid over time and the method ameliorates a steroid rebound effect associated with administration of reduced dosages of the corticosteroid.

28. A method for modulating responsiveness to a corticosteroid in a subject, comprising: selecting a subject in need of modulation of responsiveness to a corticosteroid, wherein the subject suffers from a condition normally responsive to corticosteroid therapy; and administering to the subject an interleukin-1 .beta. converting enzyme (ICE) inhibitor which antagonizes a factor that regulates production of interferon (IFN-.gamma.) in the subject, the ICE inhibitor being administered at a dosage and by a route sufficient to inhibit production of IFN-.gamma. in the subject, such that responsiveness of the subject to a corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

29. The method of claim 28, wherein the subject is resistant to a corticosteroid prior to administration of the ICE inhibitor.

30. The method of claim 28, wherein the subject is responsive to a corticosteroid prior to administration of the ICE inhibitor but exhibits increased sensitivity to the corticosteroid after administration of the ICE inhibitor.

31. The method of claim 28, wherein treatment of the subject with a corticosteroid is to be stopped and administration of the ICE inhibitor ameliorates a steroid rebound effect in the subject.

32. The method of claim 28, wherein the ICE inhibitor is an IFN-.gamma. inducing factor (IGIF) antagonist, the ICF inhibitor being administered at a dosage and by a route sufficient to inhibit IGIF activity in the subject.

33. A method for modulating responsiveness to corticosteroids in a subject comprising administering to the subject suffering from a condition normally responsive to corticosteroid therapy: an interleukin-1.beta. converting enzyme (ICE) inhibitor compound having the structure of Formula I: ##STR6## wherein R.sup.1 is hydrogen, C.sub.1 -C.sub.6 alkyl, or benzyl; R.sup.2 is --CHO, --COR.sup.a, or --CN; each R.sup.a is independently hydrogen or C.sub.1 -C.sub.6 alkyl; X is a bond, CH.sub.2, CHR.sup.5, NH, NR.sup.5, or O; R.sup.3 is aryl, substituted-aryl, heteroaryl, substituted-heteroaryl, cycloalkyl, substituted-cycloalkyl, heterocycle, or substituted-heterocycle; Y is absent, NR.sup.5, CO, S, O, SO.sub.2, --O(CHR.sup.5).sub.n --, CHR.sup.5, NR.sup.5 CO, NC(O)R.sup.5, CONR.sup.5, OCHR.sup.5, CHR.sup.5 O, SCHR.sup.5, CHR.sup.5 S, SO.sub.2 NR.sup.5, C.sub.1 -C.sub.6 alkyl, NR.sup.5 SO.sub.2, CH.sub.2 CHR.sup.5, CHR.sup.5 CH.sub.2, COCH.sub.2, or CH.sub.2 CO; R.sup.4 is absent, aryl, substituted-aryl, C.sub.1 -C.sub.8 alkyl, heteroaryl, substituted-heteroaryl, cycloalkyl, C.sub.1 -C.sub.6 alkyl, substituted-cycloalkyl, heterocycloalkyl, or substituted-heterocycloalkyl; each R.sup.5 is independently hydrogen, C.sub.1 -C.sub.6 alkyl, aryl, --(CH.sub.2).sub.n aryl, or --(CH.sub.2).sub.n cycloalkyl; each n is independently 0 to 5, m is 1 or 2, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof; and a corticosteroid, such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

34. A method for modulating responsiveness to a corticosteroid in a subject, comprising: selecting a subject in need of modulation of responsiveness to a corticosteroid, wherein the subject suffers from a condition normally responsive to corticosteroid therapy; and administering to the subject an interleukin-1.beta. converting enzyme (ICE) inhibitor compound having The structure of Formula I: ##STR7## wherein R.sup.1 is hydrogen, C.sub.1 -C.sub.6 alkyl, or benzyl; R.sup.2 is --CHO, --COR.sup.a, or --CN; each R.sup.a is independently hydrogen or C.sub.1 -C.sub.6 alkyl; X is a bond, CH.sub.2, CHR.sup.5, NH, NR.sup.5, or O; R.sup.3 is aryl, substituted-aryl, heteroaryl, substituted-heteroaryl, cycloalkyl, substituted-cycloalkyl, heterocycle, or substituted-heterocycle; Y is absent, NR.sup.5, CO, S, O, SO.sub.2, --O(CHR.sup.5).sub.n --, CHR5, NR.sup.5 CO, NC(O)R.sup.5, CONR.sup.5, OCHR.sup.5, CHR.sup.5 O, SCHR.sup.5, CHR.sup.5 S, SO.sub.2 NR.sup.5, C.sub.1 -C.sub.6 alkyl, NR.sup.5 SO.sub.2, CH.sub.2 CHR.sup.5, CHR.sup.5 CH.sub.2, COCH.sub.2, or CH.sub.2 CO; R.sup.4 is absent, aryl, substituted-aryl, C.sub.1 -C.sub.8 alkyl, heteroaryl, substituted-heteroaryl, cycloalkyl, C.sub.1 -C.sub.6 alkyl, substituted-cycloalkyl, heterocycloalkyl, or substituted-heterocycloalkyl; each R.sup.5 is independently hydrogen, C.sub.1 -C.sub.6 alkyl, aryl, --(CH.sub.2).sub.n aryl, or --(CH.sub.2).sub.n cycloalkyl; each n is independently 0 to 5, m is 1 or 2, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, the compound being administered at a dosage and by a route sufficient to inhibit production of IFN-.gamma. in the subject, such that responsiveness of the subject to a corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject.

35. A method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of pemphigus vulgaris, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, alopecia areata, allergic responses due to arthropod bite reactions, cutaneous lupus erythematosus, scleroderma, vaginitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, and erythema nodosum leprosum.

36. A method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of multiple sclerosis, autoimmune arthritis, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, autoimmune meningitis, myasthenia gravis and allergic encephalomyelitis.

37. A method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, insulin-dependent diabetes mellitus, aphthous ulcer, proctitis, Wegener's granulomatosis, chronic active hepatitis, and primary biliary cirrhosis.

38. A method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of iritis, conjunctivitis, keratoconjunctivitis, autoimmune uveitis, Graves ophthalmopathy, and uveitis posterior.

39. A method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of idiopathic thrombocytopenic purpura, autoimmune thyroiditis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, and polychondritis.

40. The method of claim 9, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of asthma, adult respiratory distress syndrome, inflammatory pulmonary syndrome, and interstitial lung fibrosis.

41. A method of claim 22, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of pemphigus vulgaris, dermatitis, atopic dermatitis, eczematous dermatitis, psoriasis, alopecia areata, allergic responses due to arthropod bite reactions, cutaneous lupus erythematosus, scleroderma, vaginitis, drug eruptions, Stevens-Johnson syndrome, leprosy reversal reactions, and erythema nodosum leprosum.

42. A method of claim 22, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of mutiple sclerosis, autoimmune arthritis, **rheumatoid arthritis**, juvenile **rheumatoid arthritis**, psoriatic arthritis, autoimmune meningitis, myasthenia gravis and allergic encephalomyelitis.

43. A method of claim 22, wherein the subject is suffering from an innumoinflammatory disease or disorder selected from the group consisting of systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, insulin-dependent diabetes mellitus, aphthous ulcer, procitis, Wegener's granulomatosis, chronic active hepatitis, and primary biliary cirrhosis.

44. A method of claim 22, wherein the subject is suffering from an inflammatory disease or disorder selected from the group consisting of ireitis, conjunctivitis, keratoconjunctivitis, autoimmune eveitis, Graves ophthalmopathy, and uveitis posterior.

45. A method of claim 22, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisiting of idiopathic thrombocytopenic purpura, autoimmune thyroiditis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, and polychondritis.

46. The method of claim 22, wherein the subject is suffering from an immunoinflammatory disease or disorder selected from the group consisting of asthma, adult respiratory distress syndrome, inflammatory pulmonary syndrome, and interstitial lung fibrosis.